

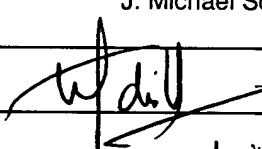
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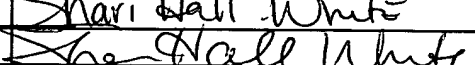
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<b>TRANSMITTAL FORM</b> (to be used for all correspondence after initial filing)	Application Number	10/087,473	
	Filing Date	March 1, 2002	
	First Named Inventor	Melissa K. Carpenter	
	Group Art Unit	TBD	
	Examiner Name	TBD	
Total Number of Pages in This Submission	14	Attorney Docket Number	090/003C

ENCLOSURES (check all that apply)		
<input type="checkbox"/> Fee Transmittal Form <input type="checkbox"/> Fee Attached <input type="checkbox"/> Amendment / Reply <input type="checkbox"/> After Final <input type="checkbox"/> Affidavits/declaration(s) <input type="checkbox"/> Extension of Time Request <input type="checkbox"/> Express Abandonment Request <input checked="" type="checkbox"/> Information Disclosure Statement <input type="checkbox"/> Certified Copy of Priority Document(s) <input type="checkbox"/> Response to Missing Parts/Incomplete Application <input type="checkbox"/> Response to Missing Parts under 37 CFR 1.52 or 1.53	<input type="checkbox"/> Assignment Papers (for an Application) <input type="checkbox"/> Drawing(s) <input type="checkbox"/> Licensing-related Papers <input type="checkbox"/> Petition <input type="checkbox"/> Petition to Convert to a Provisional Application <input type="checkbox"/> Power of Attorney, Revocation Change of Correspondence Address <input type="checkbox"/> Terminal Disclaimer <input type="checkbox"/> Request for Refund <input type="checkbox"/> CD, Number of CD(s) _____	<input type="checkbox"/> After Allowance Communication to Group <input type="checkbox"/> Appeal Communication to Board of Appeals and Interferences <input type="checkbox"/> Appeal Communication to Group (Appeal Notice, Brief, Reply Brief) <input type="checkbox"/> Proprietary Information <input type="checkbox"/> Status Letter <input checked="" type="checkbox"/> Other Enclosure(s) (please identify below): 2 Copies PTO Form 1449 (1 page); References (1); Information Disclosure Statement Pursuant to 37 CFR 1.98(d) (2 pages); 2 Copies PTO Form 1449 (4 pages)
Remarks		

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT	
Firm or Individual name	J. Michael Schiff, Registration No. 40,253
Signature	
Date	April 23, 2002

CERTIFICATE OF HAND DELIVERY			
I hereby certify that this correspondence is being delivered by hand to the U.S. Patent Office in accordance with 37 CFR 1.6(b), addressed to the Assistant Commissioner for Patents, Washington, DC 20231 on this date: April 25, 2002			
Typed or printed name	Shari Hall White		
Signature		Date	April 25, 2002

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Sh. Skell White  
Name

April 25, 2002  
Date

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the application of: Carpenter, M., et al.

Art Unit: TBD

Serial No.: 10/087,473

Examiner: TBD

Filing Date: March 1, 2002

For: DIRECT DIFFERENTIATION OF HUMAN  
PLURIPOTENT STEM CELLS AND  
CHARACTERIZATION OF DIFFERENTIATED  
CELLS

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## INFORMATION DISCLOSURE STATEMENT

## PURSUANT TO 37 CFR § 1.98(d)

Assistant Commissioner for Patents  
Washington, D.C. 20231

Dear Sir:

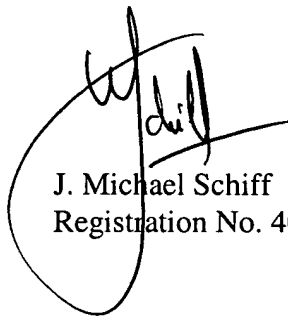
The information listed in the accompanying forms PTO-1449 may be material to examination of this application and is submitted in compliance with the duty of disclosure under 37 CFR § 1.56. The Examiner is requested to make this information of record in the application.

Copies of the information are not provided herewith, but were previously filed in parent application 09/888,309, to which this application claims priority under 35 USC § 120. The

Examiner is respectfully directed to the file for application 09/888,309 to access the information listed on the accompanying form PTO-1449. This is in compliance with the provisions of 37 CFR § 1.98(d).

This Information Disclosure Statement is not to be construed as a representation that a full search for relevant information has been made, or that the information listed on the accompanying PTO-1449 is material to patentability of the claimed invention under 37 CFR § 1.56(b).

Respectfully submitted,

A handwritten signature in black ink, appearing to read "J. Michael Schiff", is written over a large, loopy circular mark.

J. Michael Schiff  
Registration No. 40,253

GERON CORPORATION  
230 Constitution Drive  
Menlo Park, CA 94025  
*Telephone: (650) 473-7715*  
*Fax: (650) 473-8654*

April 19, 2001

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Form 1449 (modified)	Docket: 090/003C	U.S.S.N. 10/087,473
Information Disclosure Statement By Applicant  (Use Several Sheets if Necessary)	Title: Direct Differentiation of Human Pluripotent Stem Cells and Characterization of Differentiated Cells Inventors: Carpenter, M., et al.	
	Filing Date: March 1, 2002	Group: TBD

U.S. Patent Documents

Examiner Initial	Ref.	Patent No.	Filing Date	Issue Date	Class/ Subclass	Inventors:	Title:
	A	5,766,948	Nov 3/93	Jun 16/98	435/368	Gage, F.H., et al.	Method for Production of Neuroblasts
	B	5,773,255	Jun 5/95	Jun 30/98	435/70.3	Laurance, M.E., et al.	Glucose Responsive Insulin Secreting $\beta$ -Cell Lines and Method For Producing Same
	C	5,789,246	Nov 18/96	Aug 4/98	435/325	Reid, L.M., et al.	Compositions Comprising Hepatocyte Precursors
	D	5,849,553	Jun 7/95	Dec 15/98	435/172.3	Anderson, D.J., et al.	Mammalian Multipotent Neural Stem Cells
	E	5,851,832	Jun 7/95	Dec 22/98	435/368	Weiss, S., et al.	In Vitro Growth and Proliferation of Multipotent neural Stem Cells and Their Progeny
	F	5,928,947	Jun 7/95	Jul 27/99	435/455	Anderson, D.J., et al.	Mammalian Multipotent Neural Stem Cells
	G	5,968,829	Sep 5/97	Oct 19/99	435/467	Carpenter, M.	Human CNS Neural Stem Cells
	H	5,981,165	Jun 7/95	Nov 9/99	435/4	Weiss S., et al.	In Vitro Induction of Dopaminergic Cells
	I	6,040,180	May 7/97	Mar 21/00	435/377	Johe, K.	In vitro Generation of Differentiated Neurons From Cultures of mammalian Multipotent CNS Stem Cells
	J	6,090,622	Mar 31/97	Jul 18/00	435/366	Gearheart, J.D., et al.	Human Embryonic Pluripotent Germ Cells
	K	6,200,806	Jun 26/98	Mar 13/01	435/366	Thomson, J.A.	Primate Embronic Stem Cells

Foreign Patent or Published Foreign Patent Application

Examiner Initial	Ref.	Document No.	Publ. Date	Juris-diction	Title:	Translation
	L	WO 99/04775	Feb 4/99	PCT	Method of Treating Dopaminergic and Gaba-Nergic Disorders	N/A
	M	WO 99/20741	Apr 29/99	PCT	Methods and Materials for the Growth of Primate-Derived Primordial Stem Cells	N/A
	N	WO 99/43785	Sep 2/99	PCT	Derivation of Cells and Tissues from Embryonic Pre-Stem Cells for Transplantation Therapies	N/A
	O	WO 99/53021	Oct 21/99	PCT	Cell Differentiation/Proliferation and Maintnance and Uses Thereof	N/A
	P	WO 00/17323	Mar 30/00	PCT	Stable Neural Stem Cell Lines	N/A
	Q	WO 98/50526	Nov 12/98	PCT	Generation, Characterization, and Isolation of Neuroepithelial Stem Cells and Lineage Restricted Intermediate Precursor	N/A
	R	WO 99/01159	Jan 14/99	PCT	Lineage-Restricted Neuronal Precursors	N/A
	S	WO 99/28443	Jun 10/99	PCT	Lineage Restricted Glial Precursors from the Central Nervous System	N/A

Examiner	Date Considered

Examiner: Initial if citation considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.  
PTO-1449 — Page 1

**Information Disclosure  
Statement By Applicant**

(Use Several Sheets if Necessary)

Title: Direct Differentiation of Human Pluripotent Stem Cells and Characterization of Differentiated Cells  
Inventors: Carpenter, M., et al.

Filing Date: March 1, 2002

Group: TBD

## Other Documents

Examiner Initial	Ref.	Author, Title, Date, Source
	T	Andrews, et al., Retinoic Acid Induces Neuronal Differentiation of a Cloned Human Embryonal Carcinoma Cell Line in Vitro, Dev. Biol. 103:285 (1984)
	U	Bain, et al., Embryonic Stem Cells Express Neuronal Properties In Vitro, Dev. Biol. 168:342 (1995)
	V	Bain, et al., Expression of Retinoid X Receptors in P19 Embryonal Carcinoma Cells and Embryonic Stem Cells, Biochem. Biophys. Res. Commun. 200:1252 (1994)
	W	Bain, et al., Retinoic Acid Promotes Neural and Represses Mesodermal Gene Expression in Mouse Embryonic Stem Cells in Culture, Chem. and Biophys. Res. Comm. 223:691 (1996)
	X	Bieseckert, et al., Interleukin-6 is a Component of Human Umbilical Cord Serum and Stimulates Hematopoiesis in Embryonic Stem Cells in Vitro, Exp. Hematol. 21:744 (1993)
	Y	Bouwmeester, et al., Vertebrate Head Induction By Anterior Primitive Endoderm, BioEssays 19:855 (1997)
	Z	Brustle, et al., In Vitro-Generated Neural Precursors Participate in Mammalian Brain Development, Proc. Natl. Acad. Sci. USA 94:14809 (1997)
	AA	Brustle, et al., Embryonic Stem Cell-Derived Glial Precursors: A Source of Myelinating Transplants, Science 285:754 (1999)
	AB	Burkert, et al., Early Fetal hematopoietic Development From In Vitro Differentiated Embryonic Stem Cells, New Biol. 3:698 (1991)
	AC	Davidson, et al., Cell Fate and Lineage Specification in the Gastrulating Mouse Embryo, Children's Medical Res. Institute 491 (1999)
	AD	Deacon, et al., Blastula-Stage Stem Cells Can Differentiate into Dopaminergic and Serotonergic Neurons after Transplantation, Exp. Neurol. 149:28 (1998)
	AE	Dinsmore, et al., Embryonic Stem Cells Differentiated In Vitro as a Novel Source of Cells for Transplantation, Cell Transplant 5:131 (1996)
	AF	Fisher, et al., Factors Influencing the Differentiation of Embryonal Carcinoma and Embryo-Derived Stem Cells, Exp. Cell Research 182:403 (1989)
	AG	Fraichard, et al., In Vitro Differentiation of Embryonic Stem Cells into Glial Cells and Functional Neurons, J. Cell Science 108:3181 (1995)
	AH	Gendron, et al., Induction of Embryonic Vasculogenesis by bFGF and LIF In Vitro and In Vivo, Dev. Biol. 177:332 (1996)
	AI	Itskovitz-Eldor, et al., Differentiation of Human Embryonic Stem Cells into Embryoid Bodies Comprising the Three Embryonic Germ Layers, Mol. Med. 6:88 (2000)
	AJ	Kalyani, et al., Cell Lineage in the Developing Neural Tube, Biochem. Cell. Biol. 76:1051 (1998)
	AK	Keller, In Vitro Differentiation of Embryonic Stem Cells, Cell Biology 7:862 (1995)
	AL	Levinson-Dushnik, et al., Involvement of Hepatocyte Nuclear Factor 3 in Endoderm Differentiation of Embryonic Stem Cells, Mol. Cell. Biol. 17:3817 (1997)
	AM	Mujtaba, et al., Lineage-Restricted Neural Precursors Can Be Isolated from Both the Mouse neural Tube and Cultured ES Cells, Dev. Biol. 214:113 (1999)
	AN	Mummery, et al., Characteristics of Embryonic Stem Cell Differentiation: A Comparison With Two Embryonal Carcinoma Cell Lines, Cell Diff. Dev. 30:195 (1990)
	AO	Odorico, et al., Multilineage Differentiation from Human Embryonic Stem Cell Lines, Stem Cells 19:193 (2001)
	AP	Okabe, et al., Development of Neuronal Precursor Cells and Functional Postmitotic Neurons from Embryonic Stem Cells In Vitro, Mech. Dev. 59:89 (1996)

Examiner	Date Considered

Examiner: Initial if citation considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. **Include copy of this form with next communication to applicant.**

APR 26 2002

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Form 1449 (modified)	Docket: 090/003C	U.S.S.N. 10/087,473
Information Disclosure Statement By Applicant  (Use Several Sheets if Necessary)	Title: Direct Differentiation of Human Pluripotent Stem Cells and Characterization Differentiated Cells Inventors: Carpenter, M., et al.  Filing Date: March 1, 2002	
	Group: TBD	

Other Documents

Examiner Initial	Ref.	Author, Title, Date, Source
	AQ	O'Shea, Embryonic Stem Cell Models of Development, Anat. Rec. (New Anat.) 257:32 (1999)
	AR	Pedersen, Studies of In Vitro Differentiation with Embryonic Stem Cells, Reprod. Fertil. Dev. 6:542 (1994)
	AS	Rao, Multipotent and Restricted Precursors in the Central Nervous System, New Anat. 257:1 (1999)
	AT	Rathjen, et al., Formation of a Primitive Ectoderm Like Cell Population, EPL Cells, From ES Cells in Response to Biologically Derived Factors, J. Cell. Sci. 112:601 (1999)
	AU	Rathjen, et al., Properties and Uses of Embryonic Stem Cells: Prospects for Application to Human Biology and Gene Therapy, Reprod. Fertil. Dev. 10:31 (1998)
	AV	Reubinof, et al., Embryonic Stem Cell Lines From Human Blastocysts: Somatic Differentiation In Vitro, Nature Biol. 18:399 (2000)
	AW	Robertson, Derivation and Maintenance of Embryonic Stem Cell Cultures, Meth. Mol. Biol. 75:173 (1997)
	AX	Schuldiner, et al., Effects of Eight Growth Factors on the Differentiation of Cells Derived from Human Embryonic Stem Cells, PNAS 97:11307 (2000)
	AY	Strubing, et al., Differentiation of Pluripotent Embryonic Stem Cells into the Neuronal Lineage in Vitro Gives Rise to Mature Inhibitory and Excitatory Neurons, Mechanisms of Dev. 53:275 (1995)
	AZ	Seaberg, et al., Neural Determination Genes Revealed By Expression Trapping in Embryonic Stem Cells, Soc. Neurosci. (29 <sup>th</sup> Annual Meeting) 25:527 (1999)
	BA	Shamblott, et al., Derivation of Pluripotent Stem Cells from Cultured human Primordial Germ Cells, Proc. Natl. Acad. Sci. USA 95:13726 (1998)
	BB	Smith et al., Culture and Differentiation of Embryonic Stem Cells, J. Tiss. Cult. Meth. 13:89 (1991)
	BC	Thomson, et al., Embryonic Stem Cell Lines Derived from Human Blastocysts, Science 282:1145 (1998)
	BD	Trojanowski, et al., Transfectable and Transplantable Postmitotic Human Neurons: A Potential "Platform" for Gene Therapy of nervous System Diseases, Exp. Neurol. 144:92 (1997)
	BE	Tropepe, et al., Abstract 205.18: Autonomous Neural Cell Fate Specification in Mouse Embryonic Stem Cells, Soc. Neurosci. 25:527 (1999)
	BF	Tropepe, et al., Abstract 205.17: Neural Determination Genes Revealed by Expression Trapping in Embryonic Stem Cells, Soc. Neurosci. 25: 527 (1999)
	BG	Van Inzen, et al., Neuronal Differentiation of Embryonic Stem Cells, Biochim. Biophys. Acta 1312:21 (1996)
	BH	Varlet, et al., Nodal Expression in the Primitive Endoderm is Required for Specification of the Anterior Axis During Mouse Gastrulation, Development 124:1033 (1997)
	BI	Wojcik, et al., Catecholaminergic Neurons Result from Intracerebral Implantation of Embryonal Carcinoma Cells, Proc. Natl. Acad. Sci. USA 90:1305-130
	BJ	Yandava, et al., "Global" Cell Replacement is Feasible Via Neural Stem Cell Transplantation: Evidence from the Dysmyelinated Shiverer Mouse Brain, Proc. Natl. Acad. Sci. USA 96:7029 (1999)
	BK	Yao, et al., Neuronal Differentiation of P19 Embryonal Carcinoma cells in Defined Media, J. Neuroscience Res. 41:792 (1995)
	BL	Lamb, T.M., et al., Neural Induction by the Secreted Polypeptide Noggin, Science 262:713 (1993)
	BM	Lim, D.A., et al., Noggin Antagonizes BMP Signaling to Create a Niche for Adult Neurogenesis, Neuron 27:713 (2000)
	BN	Sasai, Y., et al., Regulation of Neural Induction by the Chd and Bmp-4 Antagonistic Patterning Signals in Xenopus, Nature 376:333 (1995)
Examiner		Date Considered

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PTO-1449 — Page 3

Form 1449 (modified)	Docket: 090/003C	U.S.S.N. 10/087,473
Information Disclosure Statement By Applicant  (Use Several Sheets if Necessary)	Title: Direct Differentiation of Human Pluripotent Stem Cells and Characterization of Differentiated Cells Inventors: Carpenter, M., et al. Filing Date: March 1, 2002      Group: TBD	

**Other Documents**

Examiner Initial	Ref.	Author, Title, Date, Source
	BO	Kalyani, A., et al., Cell Lineage in the Developing Neural Tube, Biochem. Cell Biol. 76:1051 (1998)
	BP	Li, M., et al., Generation of Purified Neural precursors from Embryonic Stem Cells by Lineage Selection, Current Biol., Current Science 8:971 (1998)
	BQ	Mujtaba, T., et al., Lineage-Restricted Neural Precursors Can Be Isolated from Both the Mouse Neural Tube and Cultured ES Cells, Dev. Biol. 214:113 (1999)

Examiner	Date Considered

Examiner: Initial if citation considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. **Include copy of this form with next communication to applicant.**  
 PTO-1449 — Page 4

## CERTIFICATE OF HAND DELIVERY

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She Hall White  
Name

April 25, 2002  
Date

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the application of: Carpenter, M., et al.

Art Unit: TBD

Serial No.: 10/087,473

Examiner: TBD

Filing Date: March 1, 2002

For: DIRECT DIFFERENTIATION OF HUMAN  
PLURIPOTENT STEM CELLS AND  
CHARACTERIZATION OF DIFFERENTIATED  
CELLS

## INFORMATION DISCLOSURE STATEMENT

Assistant Commissioner for Patents  
Washington, D.C. 20231

Dear Sir:

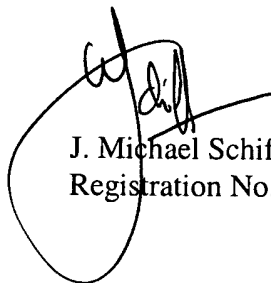
The information listed in the accompanying forms PTO-1449 may be material to examination of this application and is submitted in compliance with the duty of disclosure under 37 CFR § 1.56. The Examiner is requested to make this information of record in the application.



This Information Disclosure Statement is not to be construed as a representation that a full search for relevant information has been made, that all relevant information has been found, or that the information provided with this Statement is considered to be material to patentability of the claimed invention as defined under 37 CFR § 1.56(b).

It is believed that no fee is required for submission of this Statement, which is filed before the first Office Action on the merits of the application. Nevertheless, should a fee be required for consideration of this Statement and the listed information, the Assistant Commissioner is authorized to charge such fee to Deposit Account No. 07-1139, referencing the attorney Docket Number indicated above.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "J. Michael Schiff", is written over a large, loopy circular mark.

J. Michael Schiff  
Registration No. 40,253

GERON CORPORATION  
230 Constitution Drive  
Menlo Park, CA 94025  
*Telephone: (650) 473-7715*  
*Fax: (650) 473-8654*

April 11, 2001

Form 1449 (modified)

Docket: 090/003C

U.S.S.N. 10/087,473

**Information Disclosure  
Statement By Applicant**

(Use Several Sheets if Necessary)

Title: Direct Differentiation of Human Pluripotent Stem Cells and Characterization of Differentiated Cells

Inventors: Melissa K. Carpenter, Walter D. Funk, R. Scott Theis

Filing Date: March 1, 2002

Group: 1632

**U.S. Patent Documents**

Examiner Initial	Ref.	Patent No.	Filing Date	Issue Date	Class/ Subclass	Inventors:	Title:
None							

**Foreign Patent or Published Foreign Patent Application**

Examiner Initial	Ref.	Document No.	Publ. Date	Juris- diction	Title:	Translation
	CA	WO 98/30678	Jul 16/98	PCT	Isolated Mammalian Neural Stem Cells, Methods of Making Such Cells, and Methods of Using Such Cells	N/A

**Other Documents**

Examiner Initial	Ref.	Author, Title, Date, Source
	CB	Xu, C., et al., Feeder-free growth of undifferentiated human embryonic stem cells, Nature Biotechnology 19:971 (2001)

Examiner	Date Considered

Examiner: Initial if citation considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. **Include copy of this form with next communication to applicant.**